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CHEMISTRY

Synthesis and properties of oligonucleotides containing 4-thiothymidine, 5-methyl-2-pyrimidinone-1- β -D(2'-deoxyribose) and 2-thiothymidine

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Methods are given for the synthesis of derivatives of 4-thiothymidine ($^4\text{S}\text{T}$), 5-methyl-2-pyrimidinone-1- β -D(2'-deoxyribose) ($^4\text{H}\text{T}$) and 2-thiothymidine ($^2\text{S}\text{T}$) suitable for incorporation into oligodeoxynucleotides by the cyanoethyl phosphoramidite method. $^4\text{H}\text{T}$ and $^2\text{S}\text{T}$ are incorporated with no base protection but the sulphur atom in $^4\text{S}\text{T}$ is protected with an S-sulphenylmethyl (-SCH₃) function. This can be removed with dithiothreitol after synthesis. These T analogues have been incorporated into GACGATATCGTC, a self-complementary dodecamer containing the Eco RV recognition site (underlined), in place of the two T residues within this site. Although pure dodecamers are obtained in each case the syntheses are not as efficient as those seen when normal unmodified bases are used mainly due to the chemical reactivity of $^4\text{S}\text{T}$, $^4\text{H}\text{T}$ and $^2\text{S}\text{T}$. Some of the chemical properties of oligonucleotides containing these bases (reactivity towards NH₃) as well as their physical properties (melting temperatures, U.V., fluorescence and circular dichroism spectra) have been determined and are discussed.

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